Please delete the first sentence after the title and insert therefor --This is a continuation of application U.S. Ser. No. 08/513,278 filed on August 10, 1995, which is a continuation of application U.S. Ser. No. 08/059,027 filed on May 6, 1993, now abandoned, which is a continuation of application U.S. Ser. No. 07/786,149 filed on October 31, 1991, now issued as U.S. Pat. No. 5,216,131, which is a divisional of application U.S. Ser. No. 07/315,015 filed on February 23, 1989, now issued as U.S. Pat. No. 5,089,833, to which applications priority is claimed under 35 U.S.C. §120--.

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REMARKS

Claims 49-56 are pending in the application. No claims are added or amended. Accordingly, claims 49-56 remain in the case.

To allow consideration of the following remarks in response to the previous office action, Applicants submit the enclosed Request for Continued Prosecution and cause the finality of the previous office action to be withdrawn. Applicants respectfully request reconsideration of the outstanding objections and rejections for the reasons that follow.

Objection to the Specification

The Preliminary Amendment filed July 20, 1998 is objected to on grounds that it allegedly introduces new matter into the disclosure. In particular, the Office apparently finds that the incorporation by reference statement that is introduced by the 7/20/98 Preliminary Amendment qualifies as new matter under 35 U.S.C. §132. Although Applicants do not necessarily agree with the objection, Applicants have amended the specification to remove the incorporation by reference statement objected to by the Office. Accordingly, Applicants submit that the present amendment to the specification overcomes the objection and respectfully request that it be withdrawn.

Double Patenting Rejection Based on U.S. Pat. No. 5,216,131

Claims 49-56 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-16 of U.S. Pat. No.

5,216,131. Without intending acquiescence to the rejection, but rather to expedite prosecution, Applicants herewith submit a Terminal Disclaimer that terminally disclaims any portion of a patent granted on the present application that extends beyond the term of U.S. Pat. No. 5,216,131. Applicants submit that the Terminal Disclaimer overcomes the obviousness-type double patenting rejection based on U.S. Pat. No. 5,216,131 and respectfully request that it be withdrawn.

Double Patenting Rejection Based on U.S. Pat. No. 5,840, 844

Claims 49-56 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-13 of U.S. Pat. No. 5,840,844. Without intending acquiescence to the rejection, but rather to expedite prosecution, Applicants herewith submit a Terminal Disclaimer that terminally disclaims any portion of a patent granted on the present application that extends beyond the term of U.S. Pat. No. 5,840,844. Applicants submit that the Terminal Disclaimer overcomes the obviousness-type double patenting rejection based on U.S. Pat. No. 5,840,844 and respectfully request that it be withdrawn.

Double Patent Rejection Based on U.S. Pat. No. 5,098,833

Claims 49-56 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-33 of U.S. Pat. No. 5,098,833. The Office apparently finds that it would have been obvious to use the process of claims 16-20 and the DNA and vector of claims 1-15 and 21-32 of U.S. Pat. No. 5,098,833 to isolate the LHR protein of claims 49-56 of the present application. Although the Office Action refers to the aforementioned process, DNA and vector claims as residing in U.S. Pat. No. 5,840,844, which patent contains no such claims, Applicants assume that the Office intended to make reference to such claims in U.S. Pat. No. 5,098,833.

Applicants respectfully traverse the rejection.

The rejection is in conflict with the Final Decisions of the Board in Interference Nos. 103,052 and 103,565. In Interference No. 103,052, in which U.S. Pat. No. 5,098,833 was involved, the Redeclaration of Interference (Paper No. 25) designated claims 1-3, 5-18 and

20-33 of U.S. Pat. No. 5,098,833 as corresponding to Count 2, which reads as follows:

A DNA isolate encoding a polypeptide having an amino acid sequence selected from the group consisting of:

a) the amino acid sequence for the human LHR shown in Figure 1 of U.S. Patent 5,098,833; and

b) the amino acid sequence for the human LAM-1 protein shown in Figure 2 of U.S. Patent Application 08/036,453.

The above-described designation of claims was not challenged and became final upon Judgment (Paper No. 130) awarding the subject matter of Count 2 to senior party Thomas F. Tedder following junior party Lasky et al.'s filing of a concession of priority (Paper No. 125). Party Tedder and party Weissman filed a request that the APJ exercise authority under 37 C.F.R. §1.642 to add U.S. Pat. No. 5,216,131 to Interference No. 103,052. In a Decision on Motions (Paper No. 68), the APJ denied the request. The APJ's denial of the request was not challenged and became final upon entry of Judgment for party Tedder.

In Interference No. 103,516, in which U.S. Pat. No. 5,098,833 was involved, the Declaration of Interference (Paper No. 23) designated claims 1-2, 4-17, and 19-32 as corresponding to Count 1, which reads as follows:

A DNA isolate encoding a polypeptide having the amino acid sequence for the murine LHR shown in Figure 2 of U.S. Patent 5,098,833.

The above-described designation of claims was not challenged and became final upon Judgment (Paper No. 8) awarding the subject matter of Count 1 to senior party Lasky et al. following junior party Weissman et al.'s filing of a request pursuant to 37 C.F.R. §1.662 for entry of adverse judgment (Paper No. 7).

In Interference No. 103,565, in which U.S. Pat. No. 5,216,131 was involved, the

Redeclaration of Interference (Paper No. 17) designated claims 1-7 and 9-15 of U.S. Pat. No. 5,216,131 as corresponding to Count 2, which reads as follows:

> An essentially purified human LHR (HuLHR) comprising an amino acid sequence encoded by the DNA sequence indicated in Fig. 1 of U.S. Patent 5,216,131,
>
> or
>
> An essentially purified human lymphocyte-associated cell surface protein comprising an amino acid sequence encoded by the DNA sequence indicated in Fig. 2 of U.S. application 07/983,606.

The above-mentioned designation of claims was not challenged and became final upon Judgment (Paper No. 122) awarding the subject matter of Count 2 to junior party Lasky et al. following senior party Tedder's filing of a concession of priority.

As shown above, the Board designated the claims of U.S. Pat. No. 5,098,833 as corresponding to Count 2 of Interference No. 103,052 and/or Count 1 of Interference No. 103,516, which Counts recite DNA encoding human LHR and DNA encoding murine LHR, respectively. The Board declined party Tedder's and party Weissman's joint request that the APJ exercise authority under 37 C.F.R. §1.642 to add U.S. Pat. No. 5,216,131 to Interference No. 103,052. In addition, the Board did not designate any of the claims of U.S. Pat. No. 5,216,131 as corresponding to Count 1 in Interference No. 103,516. Instead, the Board designated the claims of U.S. Pat. No. 5,216,131 as corresponding to Count 2 of Interference No. 103,565, which Count recites human LHR.

In declining to add U.S. Pat. No. 5,216,131 to Interference Nos. 103,052 or 103,516, the Board necessarily found that the claims of U.S. Pat. No. 5,216,131 do not claim the same

patentable subject matter as Count 2 in Interference No. 103,052 or Count 1 in Interference No. 103,516. Under 37 C.F.R. §1.601(n), invention "A" is the same patentable invention as invention "B" when invention "A" is the same as or obvious in view of invention "B" assuming invention "B" is prior art with respect to invention "A". Accordingly, the Board's finding must have been based on a determination that the human LHR and the murine LHR claimed in the claims of U.S. Pat. No. 5,216,131 are not the same as or obvious in view of the DNA encoding human LHR recited in Count 2 in Interference No. 103,052 or the DNA encoding murine LHR recited in Count 1 in Interference No. 103, 516 assuming that such DNAs are prior art with respect to the human LHR and the murine LHR claimed in the claims of U.S. Pat. No. 5,216,131.

As stated above, the Office apparently finds that the human LHR claimed in claims 49-56 of the present application would have been obvious in view of the DNA, vectors and processes recited in the claims of U.S. Pat. No. 5,098,833. According to the Office's reasoning in support of the rejection, DNA encoding human LHR would render obvious the human LHR of claims 49-56 in the present application assuming that such DNA is prior art against claims 49-56. This position is in conflict with the Board's finding that the human LHR claimed in the claims of U.S. Pat. No. 5,216,131 is not the same as or obvious in view of the DNA encoding human LHR recited in Count 2 in Interference No. 103,052.

Since the Board's finding is law of the case, any action taken by the Office in examination of the application must be consistent therewith. As shown above, the obviousness-type double patenting rejection over U.S. Pat. No. 5,098,833 is based on a position that is inconsistent with the Board's finding. Accordingly, the rejection is improper and should be withdrawn.

Rejection under 35 U.S.C. §102

Claims 49-51 and 54-56 are rejected under 35 U.S.C. §102 as allegedly being anticipated by Woodruff and Clarke, Ann. Rev. Immunol., 5: 201-222 (1987), hereafter

"Woodruff." The Office apparently finds that Woodruff disclosed the human LHR. In support of this finding, the Office states that the human LHR disclosed in Woodruff inherently has the same structure and amino acid sequence as the polypeptide of the claimed invention because Woodruff identified the human LHR by using the same techniques that were used in mouse and rat and because Woodruff isolated the human LHR from T-cells like other LHRs.

Applicants respectfully traverse the rejection.

Contrary to the apparent position of the Office, the teaching of Woodruff would have indicated that the "HEBF-LN" preparation of Woodruff was not human LHR. Woodruff reported that Woodruff's HEBF-LN preparation bound to the high endothelial venules (HEV) of peripheral lymph nodes but did not bind to the HEV of mesenteric lymph nodes. In particular, Woodruff found that rat thoracic duct lymphocytes (TDLs) expressing the A.11 antigen (HEBF-LN) accumulated in rat cervical lymph nodes but exhibited little tendency to migrate into rat mesenteric lymph nodes (see Fig. 4 on p. 216 and the paragraph bridging pp. 215-216 of Woodruff). Woodruff also found that the anti-human HEBF-LN monoclonal antibody 3.A.7 inhibited the binding of human peripheral blood lymphocytes (PBLs) to the HEV of rat peripheral lymph nodes but did not inhibit the binding of PBLs to the HEV of rat mesenteric lymph nodes (see Table 3 on p. 218 and the discussion of the data of Table 3 on p. 217 of Woodruff). Thus, the data of Woodruff would have indicated that Woodruff's HEBF-LN is involved in lymphocyte homing to the HEV of peripheral lymph nodes and is not involved in lymphocyte homing to the HEV of mesenteric lymph nodes.

As reported in Watson, et al., Nature, 349: 164-167 (1991), hereafter "Watson," newly cited, a copy of which is enclosed with the Supplemental Information Disclosure Statement submitted herewith, the Mel-14 monoclonal antibody and a soluble immunoglobulin (IgG) chimera of the murine homing receptor (mHRLEC-IgG) each inhibited the passage of ^{51}Cr-labeled lymphocytes to peripheral and mesenteric lymph nodes, but not Peyer's patches, in mouse (see Fig. 2a on p. 165 and the paragraph bridging pp. 164-166 of Watson). Thus, Watson taught that homing receptor targets the migration of lymphocytes to HEV of both

peripheral lymph nodes and mesenteric lymph nodes.

In addition, Ley, et al., Blood, 77: 2553-2555 (1991), hereafter "Ley," newly cited, a copy of which is enclosed with the Supplemental Information Disclosure Statement submitted herewith, taught that microinfusion of an IgG chimera of the murine homing receptor (LEC-IgG) or polyclonal antiserum against murine homing receptor (LEC-CAM 1) into mesenteric endothelial venules of rat greatly reduced the number of rolling leukocytes observed (see Fig. 1 and the first paragraph under "Results" on page 2554 of Ley). Ley concluded that the inhibitory effects of murine LEC-IgG and anti-murine LEC-CAM 1 antiserum on leukocyte rolling was caused by interference with the interaction between murine homing receptor (LEC-CAM 1) and its endothelial ligand in the mesenteric venules of rat (see the last paragraph on p. 2555 of Ley).

As shown above, Woodruff taught that HEBF-LN was involved in the homing of lymphocytes to HEV of peripheral lymph nodes but was not involved in the homing of lymphocytes to HEV of mesenteric lymph nodes. Since the murine lymphocyte homing receptor binds to ligand on the HEV of both peripheral lymph nodes and mesenteric lymph nodes, as shown in the discussion of Watson and Ley above, and since the murine lymphocyte homing receptor is the murine homolog of the human lymphocyte homing receptor, it is reasonable to expect that the human homolog also binds to ligand on the HEV of both peripheral and mesenteric lymph nodes. The HEBF-LN of Woodruff does not possess the homing activity for peripheral and mesenteric lymph node HEV that would be reasonably expected of the human lymphocyte homing receptor. Accordingly, it is not reasonable to conclude that Woodruff's HEBF-LN is the same as the claimed lymphocyte homing receptor. In fact, the data of Woodruff are a strong indication that Woodruff's HEBF-LN is not the same as the claimed lymphocyte homing receptor.

Even if it is assumed that the HEBF-LN preparation of Woodruff contains human lymphocyte homing receptor, the disclosure of Woodruff would not have enabled the ordinarily skilled artisan to make the HEBF-LN preparation of Woodruff. Woodruff's only description of how Woodruff made HEBF-LN is as follows:

> Initial experiments showed that rabbit-anti-rat $HEBF_{LN}$ antibody surface labeled 60-70% of PBL of healthy donors. However, attempts to block PBL-HEV binding with this reagent were not successful. Nevertheless, affinity chromatography studies using this polyclonal antibody led to the isolation of biologically active HEBF from detergent-solubilized PBL and soluble HEBF from sera of healthy adults (L.M. Clarke, J.J. Woodruff, unpublished observations). (p. 217 of Woodruff)

The above-quoted description of Woodruff's methods suffers from numerous deficiencies. The text fails to provide any guidance on how Woodruff raised the rabbit anti-rat $HEBF_{LN}$ polyclonal antibody. Likewise, Woodruff provides no direction on how to make the affinity chromatography column using the polyclonal antibody. Woodruff also fails to disclose what conditions and procedures were used to process human serum samples and human PBL lysate samples by affinity chromatography. In particular, Woodruff does not teach how to (1) prepare the human serum samples and human PBL lysate samples for chromatography (2) adsorb the samples to solid phase in the chromatography column (which requires knowledge of the equilibration, diluent and wash buffers used, including all physical characteristics of these solutions such as the buffering agents, concentrations, ionic strength, pH, etc.) (3) elute adsorbed material from solid phase in the column (which requires knowledge of the elution buffer used) or (4) recover the elution fractions from the column (which requires knowledge of the flow rate, fraction volume and fraction collection pattern used).

Since Woodruff used a polyclonal antibody as the affinity reagent, the product recovered from Woodruff's affinity chromatography effort was likely to be a complex mixture of proteins. In fact, it is likely that abundant human cellular and serum proteins present at high concentrations in the samples will react with the polyclonal antibody and will outcompete any $HEBF_{LN}$ material in the purification procedures, resulting in poor or even undetectable yields of the $HEBF_{LN}$. Thus, it was essential to detail the exact procedures and methods used by Woodruff in order to provide the practitioner with any chance of duplicating Woodruff's results. As shown above, Woodruff failed to provide any of the details necessary for the practitioner to make Woodruff's $HEBF_{LN}$. Accordingly, Woodruff does not satisfy the requirements of a prior art reference and does not anticipate the claims.

The Office indicates that Jalkanen and Butcher, Blood, 66: 577-582 (1985), Jalkanen, et al., Ann. Rev. Med., 38: 467-476 (1987), Jalkanen, et al., Eur. J. Immunol., 16: 1195-1202 (1986), and Jalkanen, et al., J. Cell Biol., 105: 983-990 (1987), hereafter collectively referred to as "the Jalkanen references," are not relied upon but considered pertinent to Applicants' disclosure. The Jalkanen references only describe the Hermes antigen (CD44). As taught by Bowen, et al., J. Cell Biol., 109: 421-427 (1989), hereafter "Bowen," newly cited, a copy of which is enclosed with the Supplemental Information Disclosure Statement submitted herewith, there is no significant sequence homology between the human lymphocyte homing receptor sequence and the sequence of the Hermes antigen disclosed in the Jalkanen references (see the first full paragraph in the right column on p. 426 of Bowen). Therefore, the Jalkanen references add nothing to Woodruff and do not provide support for an art rejection against the claims.

In view of the above, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b).

In light of the present amendment and arguments, Applicants believe that the application is in condition for allowance and earnestly solicit a Notice to that effect. If the Examiner has any question concerning this communication, he should feel free to contact the undersigned attorney at the telephone number indicated below.

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